switched), however, show a statistically greater proportion of high-risk patients in the consistent treatment group (see Table 1 of White et al. [1]). Thus, similarity of the 2 groups is not a strength of the study as suggested.

Removal of the bivalirudin plus glycoprotein (GP) IIb/IIIa group from this post-hoc analysis effectively removes a large population that could have increased bleeding complications, and it would be interesting to see whether the end points could be maintained if the switch from heparin to bivalirudin plus GP IIb/IIIa inhibitors was added to the population studied.

Bivalirudin was compared with heparin plus a GP IIb/IIIa inhibitor. Although recommended by guidelines, in the setting described, the proportion of patients being placed on GP IIb/IIIa inhibitors in real-world practice is much lower (i.e., approximately 25% in the U.S. [2] and 5% in Australia [3]).

Although one could expect some mortality benefit in the switched group, because of reduced bleeding over a length of time as in the ISAR (Innovative Stratification of Arrhythmic Risk) trials (4), the cost effectiveness of bivalirudin is a critical question when considering popular use.

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REFERENCES

1. White HD, Chew DP, Hoekstra JP, et al. Safety and efficacy of switching from either unfractionated heparin or enoxaparin to bivalirudin inpatients with non–ST-segment elevation in acute coronary syndromes managed with an invasive strategy: results from the ACUITY (Acute Catheterization and Urgent Intervention Triage strategY) trial. J Am Coll Cardiol 2008;51:1734–41.
2. Peterson ED, Pollack CV Jr., Roe MT, et al., for Barron National Registry of Myocardial Infarction (NRMI) 4 Investigators. Early use of glycoprotein IIb/IIIa inhibitors in non–ST-elevation acute myocardial infarction: observations from the National Registry of Myocardial Infarction. J Am Coll Cardiol 2003;42:45–53.
3. Walters DL, Aroney CN, Chew DP, et al. Variations in the application of cardiac care in Australia. Med J Aust 2008;188:218–23.
4. Ndrepepa G, Berger PB, Mehilli J, et al. Periprocedural bleeding and 1 year outcome after percutaneous coronary interventions: appropriateness of including bleeding as a component of a quadruple end point. J Am Coll Cardiol 2008;51:690–7.

Reply

We would like to thank Drs. Mishra and Walters for their interest in our work (1). As they accurately point out, there were differences in 2 of the more than 20 baseline characteristics. However, although patients in the heparin plus glycoprotein IIb/IIIa inhibitor (GPI) group more frequently had increased creatine kinase-myocardial band, troponin levels, or electrocardiogram changes, multivariate logistic regression confirmed the results of the univariate analysis. This adjusted analysis demonstrated that switching from heparin plus a GPI to bivalirudin monotherapy resulted in similar rates of composite ischemia (odds ratio [OR]: 0.97; 95% confidence interval [CI]: 0.76 to 1.23; $p = 0.77$), and significantly less non-coronary artery bypass graft major bleeding (OR: 0.47; 95% CI: 0.34 to 0.66; $p < 0.0001$) and net clinical events (OR: 0.76; 95% CI: 0.62 to 0.94; $p = 0.01$).

Regarding why we elected not to display the results of the bivalirudin plus GPI group, in the main ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial (2), bivalirudin plus GPI showed no incremental benefit over bivalirudin alone in terms of reducing ischemia but did result in more bleeding. Given these facts, the more expensive bivalirudin plus GPI regimen is unlikely to enter routine clinical practice and, thus, we did not include these data in the article.

The third point Drs. Mishra and Walters make is that the ACUITY trial was designed to assess the addition of a treatment (bivalirudin) to guideline-recommended therapy. We believe that this is the appropriate way to perform trials; it would be detrimental for patients to test new treatments in the absence of guideline-recommended therapies.

Finally, in respect to cost effectiveness, preliminary analysis shows bivalirudin to be very cost effective. A prospective analysis (3) showed that 30-day costs were lowest with bivalirudin monotherapy compared with heparin plus GPI (cost savings ranging from $123 per patient with bivalirudin monotherapy vs. heparin + GPI administration in the catheterization laboratory to $422 per patient with bivalirudin monotherapy vs. heparin + upstream GPI).

Thus, adjusted analysis of the switch cohort demonstrates that the results with bivalirudin monotherapy remain consistent despite slight differences in baseline characteristics. The present study supports the safety and efficacy of switching to bivalirudin from unfractionated heparin or enoxaparin in moderate- and high-risk patients with non–ST-segment elevation acute coronary syndromes and preserves the 50% reduction in major bleeding seen with bivalirudin, with comparable rates of ischemia and, thus, improved overall patient outcomes.

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REFERENCES

1. White HD, Chew D, Hoekstra J, et al. Safety and efficacy of switching from either unfractionated heparin or enoxaparin to bivalirudin in patients with non–ST-segment elevation acute coronary syndromes managed with an invasive strategy: results from the ACUITY (Acute Catheterization and Urgent Intervention Triage strategY) trial. J Am Coll Cardiol 2008;51:1734–41.
2. Stone GW, McLaurin BT, Cox DA, et al. Bivalirudin for patients with acute coronary syndromes. N Engl J Med 2006;355:2203–16.
3. Pinto DS, Stone GW, Shi C, et al. Economic evaluation of bivalirudin with or without glycoprotein IIb/IIIa inhibition versus heparin with routine glycoprotein IIb/IIIa inhibition for early invasive management of acute coronary syndromes. Paper presented at: the American College of Cardiology 57th Annual Scientific Sessions; March 29 to April 1, 2008; Chicago, IL.